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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,616	06/09/2006	Zee Upton	FAK8011	2998
	LI, SUNDHEIM, COVELL & TUMMINO L.L.P. AST NINTH STREET, SUITE 1700 LAND, OH 44114		EXAMINER	
1300 EAST NII			SGAGIAS, MAGDALENE K	
CLEVELAND,	ОП 44114		ART UNIT PAPER NUMBER	
			1632	
			MAIL DATE	DELIVERY MODE
			10/11/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

	Application No.	Applicant(s)					
Office Action Comment	10/565,616	UPTON ET AL.					
Office Action Summary	Examiner	Art Unit					
	MAGDALENE SGAGIAS	1632					
The MAILING DATE of this communication app Period for Reply	ears on the cover sheet with the c	orrespondence ad	ldress				
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).							
Status							
1) Responsive to communication(s) filed on 07 Ju	ne 2011.						
	action is non-final.						
3) An election was made by the applicant in response		set forth during the	e interview on				
	; the restriction requirement and election have been incorporated into this action.						
	4) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is						
closed in accordance with the practice under E	x parte Quayle, 1935 C.D. 11, 45	3 O.G. 213.					
Disposition of Claims							
5) Claim(s) 1-6, 8-28, 35-37 is/are pending in the	application.						
· · · · · · · · · · · · · · · · · · ·	5a) Of the above claim(s) <u>3,4,6,8-20,24-28,35 and 36</u> is/are withdrawn from consideration.						
6) Claim(s) is/are allowed.							
7) Claim(s) <u>1,2,5,21-23 and 37</u> is/are rejected.	· · · ———						
8) Claim(s) is/are objected to.							
9) Claim(s) are subject to restriction and/or	election requirement.						
Application Papers	·						
	•						
10) The specification is objected to by the Examiner.							
,	1) The drawing(s) filed on <u>01/24/2006</u> is/are: a) accepted or b) objected to by the Examiner.						
	Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).						
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).							
12) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.							
Priority under 35 U.S.C. § 119							
13) Acknowledgment is made of a claim for foreign	priority under 35 U.S.C. § 119(a)	-(d) or (f).					
a) ☐ All b) ☐ Some * c) ☐ None of:	a) ☐ All b) ☐ Some * c) ☐ None of:						
1. Certified copies of the priority documents							
2. Certified copies of the priority documents have been received in Application No							
3. Copies of the certified copies of the priority documents have been received in this National Stage							
application from the International Bureau (PCT Rule 17.2(a)).							
* See the attached detailed Office action for a list of the certified copies not received.							
Au							
Attachment(s)							
1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) Paper No(s)/Mail Date							
3) Information Disclosure Statement(s) (PTO/SB/08) 5) Notice of Informal Patent Application							
Paper No(s)/Mail Date	6)						

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DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/07/2011 has been entered.

Applicant's arguments filed 06/07/2011 have been fully considered. The amendments to the claims dated 06/07/2011 have been entered. Claims 1-6, 8-28, 35-37 are pending. Claims 7, 29-34, 38 are canceled. Claims 3-4, 6, 8-20, 24-28, 35-36 are withdrawn. Claims 1-2, 5, 21-23, and 37 are under consideration.

Claim Objections

Claims 1 and 23 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, claim 1 recites "VN fragment comprising amino acid residues 1-52 of mature VN", while depended claim 23 recites a broader range of: "wherein said vitronectin (VN).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1-2, 5, 21-23, and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "amino acid residues 1-52 of mature VN". It is not clear whether the amino acid sequences 1-52 of mature VN will be the same the amino acid sequences 1-52 of mature VN in all animal species. The recitation of specific amino acid residues is relative to where the start of a peptide is, and can contain allelic variations even within a species.

Claims 2, 5, 21-23, and 37 depend from claim 1.

Claim Rejections - 35 USC § 112

The rejection of claims **1-2**, **5**, **21-23**, **37** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is <u>withdrawn</u> in view of the amendment dated to claim 1 in steps (i)(a) and (ii), where an IGFBP not present in an <u>IGF-II/VN</u> synthetic chimera is not required.

To the extent the claimed compositions are not described in the instant disclosure, claims **1-2**, **5**, **21-23**, **37** are also rejected under 35 U.S.C. 112, first paragraph, is <u>withdrawn</u> in view of the amendment to claim 1 in steps (i)(a) and (ii) where an IGFBP not present in an <u>IGF-II/VN</u> synthetic chimera is not required.

Claim Rejections - 35 USC § 112/New Matter

The rejection of claims **1-2**, **5**, **21-23**, **37** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is <u>withdrawn</u> in view of the amendment dated 06/07/2011, where an IGFBP not present in an <u>IGF-II/VN</u> synthetic chimera is not required.

To the extent the claimed compositions are not described in the instant disclosure, claims 1-2, 5, 21-23, 37 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since the applicants disclosure do not teach a composition that is adequately described in the specification is <u>withdrawn</u> in view of the amendment dated 06/07/2011, where an IGFBP not present in an <u>IGF-II/VN</u> synthetic chimera is not required.

Claim Rejections - 35 USC § 112

The rejection of claims **1-2**, **5**, **21-23**, **37** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is <u>withdrawn</u> in view of the amendment dated 06/07/2011, where an a_v integrin-receptor binding vitronecin (VN) fragment comprising amino acid residues 1-52 of mature VN.

Claims 2, 5, 21-23, and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims functional amino acid sequences 1-52 of mature VN and insulin-like growth factor. The claims read on a broad genus of sequences.

The written description requirement for a genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicants were in possession of the claimed invention. In the instant case, the specification does not sufficiently describe a representative number of functional mutants of vitronectin of amino acid sequences 1-52 of mature vitronectin from different species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claim a functional amino acid sequences 1-52 of mature VN and insulin-like growth factor by function only, without any disclosed or known correlation between the elements and their function. The specification does not teach how to make all variable sequences of all animal species of amino acid sequences 1-52 of mature VN and insulin-like growth factor and still have it function to an a_v integrin-receptor binding vitronectin. The BLAST sequence alignment among the various species of amino acid sequences 1-52 of mature VN shows that there is no 100% homology among the various species (See Blast alignment below). Furthermore, the numbering of amino acids depends upon the start of the peptide, which can differ between species or have allelic variations within the same species.

The skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification because the specification does not disclose amino acid sequences 1-52 of mature VN and insulin-like growth factor.

The state of the art at the time of filing does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the

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art that allows one to envision a representative number of functional amino acid sequences that comprise amino acids 1-52 of mature VN and insulin-like growth factor variable sequences by disclosing structural or functional features of the sequences that are encompassed by sequences that contain amino acid residues 1-52 of mature VN from any animal species and insulin-like growth factor so that one of skill in the art could envision the claimed invention. Thus the skilled artisan cannot consult the art at the time of filing to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the state of the art at the time of filing teaches a structure-function relationship for a representative number of functional variable of amino acid residues 1-52 of mature VN from any species and insulin-like growth factor. As a result, the skilled artisan would not be able to envision the claimed invention. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

BLAST alignment: amino acid sequences 1-52 of mature VN.

```
pdb|10C0|B
                  Chain B, Plasminogen Activator Inhibitor-1 Complex With
Somatomedin
B Domain of Vitronectin
pdb|1S4G|A Chain A, Somatomedin-B Domain Of Human Plasma Vitronectin.
pdb|1SSU|A
              Chain A, Structural And Biochemical Evidence For Disulfide
Bond
Heterogeneity In Active Forms Of The Somatomedin B Domain
Of Human Vitronectin
Length=51
Score = 61.2 bits (147), Expect = 5e-15, Method: Compositional matrix
Identities = 27/33 (82%), Positives = 29/33 (88%), Gaps = 0/33 (0%)
Query 20 DQESCKGRCTQGFMASKKCQCDELCTYYQSCCA
          DQESCKGRCT+GF
                          KKCQCDELC+YYQSCC
Sbjct 1
          DQESCKGRCTEGFNVDKKCQCDELCSYYQSCCT 33
```

```
pdb|2JQ8|A
                  Chain A, Solution Structure Of The Somatomedin B Domain
From
Vitronectin Produced In Pichia Pastoris
Length=53
Score = 60.8 bits (146), Expect = 8e-15, Method: Compositional matrix
adjust.
Identities = 27/33 (82%), Positives = 29/33 (88%), Gaps = 0/33 (0%)
Query 20 DQESCKGRCTQGFMASKKCQCDELCTYYQSCCA 52
          DQESCKGRCT+GF KKCQCDELC+YYQSCC
Sbjct 1 DQESCKGRCTEGFNVDKKCQCDELCSYYQSCCT 33
                  Chain B, Structure Of Urokinase Receptor, Urokinase And
Vitronectin
Complex
pdb|3BT2|B Chain B, Structure Of Urokinase Receptor, Urokinase And
Vitronectin
Complex
Length=40
Score = 58.2 bits (139), Expect = 6e-14, Method: Compositional matrix
adjust.
Identities = 26/32 (81%), Positives = 28/32 (88%), Gaps = 0/32 (0%)
Query 21 QESCKGRCTQGFMASKKCQCDELCTYYQSCCA 52
          QESCKGRCT+GF
                       KKCQCDELC+YYQSCC
Sbjct 1
          QESCKGRCTEGFNVDKKCQCDELCSYYQSCCT 32
    pdb|3NKM|A Crystal Structure Of Mouse Autotaxin
pdb|3NKN|A
              Chain A, Crystal Structure Of Mouse Autotaxin In Complex With
14:0-Lpa
pdb|3NKO|A
               Chain A, Crystal Structure Of Mouse Autotaxin In Complex With
16:0-Lpa
pdb|3NKP|A
               Chain A, Crystal Structure Of Mouse Autotaxin In Complex With
18:1-Lpa
pdb|3NKQ|A
               Chain A, Crystal Structure Of Mouse Autotaxin In Complex With
18:3-Lpa
pdb|3NKR|A
               Chain A, Crystal Structure Of Mouse Autotaxin In Complex With
22:6-Lpa
```

Length=831

E value Score

Percent identity

Query start

position Subject start position

Score = 37.0 bits (84), Expect = 1e-04, Method: Composition-based stats. Identities = 18/47 (38%), Positives = 25/47 (53%), Gaps = 3/47 (6%)

Query 6 PFFILALVAWVSLADQESCKGRCTQ-GFMASKKCQCDELCTYYQSCC 51
P +L+ W + + SCKGRC + + C+CD LC Y SCC

Sbjct 7 PPTVLSDSPWTNTSG--SCKGRCFELQEVGPPDCRCDNLCKSYSSCC 51

Score = 24.3 bits (51), Expect = 4.6, Method: Composition-based stats. Identities = 10/30 (33%), Positives = 11/30 (37%), Gaps = 0/30 (0%)

Query 22 ESCKGRCTQGFMASKKCQCDELCTYYQSCC 51 E K RC + C C E C CC

Sbjct 66 ECTKDRCGEVRNEENACHCSEDCLSRGDCC 95

> pdb|2XR9|A Chain A, Crystal Structure Of Autotaxin (Enpp2)
Length=827

Sort alignments for

this subject sequence by:

E value Score

Percent identity

Query start

position Subject start position
Score = 36.6 bits (83), Expect = 1e-04, Method: Composition-based stats.
Identities = 18/47 (38%), Positives = 25/47 (53%), Gaps = 3/47 (6%)

Query 6 PFFILALVAWVSLADQESCKGRCTQ-GFMASKKCQCDELCTYYQSCC 51 P +L+ W + + SCKGRC + + C+CD LC Y SCC

Sbjct 7 PPTVLSDSPWTNTSG--SCKGRCFELQEVGPPDCRCDNLCKSYSSCC 51

Score = 24.3 bits (51), Expect = 4.9, Method: Composition-based stats. Identities = 10/30 (33%), Positives = 11/30 (37%), Gaps = 0/30 (0%)

Query 22 ESCKGRCTQGFMASKKCQCDELCTYYQSCC 51
E K RC + C C E C CC
Sbjct 66 ECTKDRCGEVRNEENACHCSEDCLSRGDCC 95

```
Sort alignments for
```

this subject sequence by:

E value Score

Percent identity

Query start

position Subject start position

Score = 36.6 bits (83), Expect = 2e-04, Method: Composition-based stats. Identities = 18/47 (38%), Positives = 25/47 (53%), Gaps = 3/47 (6%)

Query 6 PFFILALVAWVSLADQESCKGRCTQ-GFMASKKCQCDELCTYYQSCC 51
P +L+ W + + SCKGRC + + C+CD LC Y SCC

Sbjct 42 PPTVLSDSPWTNTSG--SCKGRCFELQEVGPPDCRCDNLCKSYSSCC 86

Score = 23.9 bits (50), Expect = 5.2, Method: Composition-based stats. Identities = 10/30 (33%), Positives = 11/30 (37%), Gaps = 0/30 (0%)

Query 22 ESCKGRCTQGFMASKKCQCDELCTYYQSCC 51 E K RC + C C E C CC

Sbjct 101 ECTKDRCGEVRNEENACHCSEDCLSRGDCC 130

Transferase Homolog: Insight Into Molecular Control Of Intracellular Glycosylation

Score = 25.4 bits (54), Expect = 1.6, Method: Composition-based stats. Identities = 12/26 (46%), Positives = 15/26 (58%), Gaps = 0/26 (0%)

Query 12 LVAWVSLADQESCKGRCTQGFMASKK 37 VAW+ LAD E G T G MA ++

Sbjct 23 FVAWLMLADAELGMGDTTAGEMAVQR 48

pdb|2VSY|B
Chain B, Xanthomonas Campestris Putative Ogt (Xcc0866),
Apostructure

With Udp-Glenac Phosphonate Analogue

7 more sequence titles

```
Chain A, Substrate And Product Analogues As Human O-Glcnac
Transferase
Inhibitors.
pdb|2XGM|B Chain B, Substrate And Product Analogues As Human O-Glcnac
Transferase
Inhibitors.
pdb|2XGO|A
              Chain A, Xcogt In Complex With Udp-S-Glcnac
pdb|2XGO|B
              Chain B, Xcogt In Complex With Udp-S-Glcnac
pdb | 2XGS | A
               Chain A, Xcogt In Complex With C-Udp
pdb|2XGS|B
               Chain B, Xcogt In Complex With C-Udp
Length=568
Score = 25.4 bits (54), Expect = 1.6, Method: Composition-based stats.
Identities = 12/26 (46%), Positives = 15/26 (58%), Gaps = 0/26 (0%)
Query 12 LVAWVSLADQESCKGRCTQGFMASKK 37
          VAW+ LAD E G T G MA ++
Sbjct 23 FVAWLMLADAELGMGDTTAGEMAVQR 48
    pdb|1KEA|A Chain A, Structure Of A Thermostable Thymine-Dna
Glycosylase
Length=221
GENE ID: 3355209 pFV1 p10 | hypothetical protein
[Methanothermobacter thermautotrophicus] (10 or fewer PubMed links)
Score = 23.9 bits (50), Expect = 6.0, Method: Composition-based stats.
Identities = 7/15 (47%), Positives = 11/15 (73%), Gaps = 0/15 (0%)
           KKCQCDELCTYYQSC 50
Query 36
           +KC
                 +LC+YY+ C
Sbjct 205 EKCGMSKLCSYYEKC 219
    pdb|2AI0|L Chain L, Anti-Cocaine Antibody 7.5.21, Crystal Form Iii
pdb|2AI0|M Chain M, Anti-Cocaine Antibody 7.5.21, Crystal Form Iii
pdb|2AI0|N
              Chain N, Anti-Cocaine Antibody 7.5.21, Crystal Form Iii
pdb|2AI0|0
              Chain O, Anti-Cocaine Antibody 7.5.21, Crystal Form Iii
Length=217
Score = 23.5 bits (49), Expect = 6.8, Method: Composition-based stats.
Identities = 10/20 (50%), Positives = 12/20 (60%), Gaps = 0/20 (0%)
Query 16 VSLADQESCKGRCTQGFMAS 35
          VSL DQ S
                    RC+Q + S
Sbjct 13 VSLGDQASISCRCSQSIVKS 32
```

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pdb|2A1W|L Chain L, Anti-Cocaine Antibody 7.5.21, Crystal Form I
pdb|2A1W|M Chain M, Anti-Cocaine Antibody 7.5.21, Crystal Form I
Length=216
Score = 23.5 bits (49), Expect = 7.4, Method: Composition-based stats.
Identities = 10/20 (50%), Positives = 12/20 (60%), Gaps = 0/20 (0%)
Query 16 VSLADQESCKGRCTQGFMAS 35
          VSL DQ S
                   RC+Q + S
Sbjct 13 VSLGDQASISCRCSQSIVKS 32
> pdb|2A77|L  Chain L, Anti-Cocaine Antibody 7.5.21, Crystal Form Ii
Length=216
Score = 23.5 bits (49), Expect = 7.5, Method: Composition-based stats.
Identities = 10/20 (50%), Positives = 12/20 (60%), Gaps = 0/20 (0%)
Query 16 VSLADQESCKGRCTQGFMAS 35
          VSL DQ S RC+Q + S
Sbjct 13 VSLGDQASISCRCSQSIVKS 32
```

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1-2 under 35 U.S.C. 102(b) as being anticipated by Upton et al [Endocrinology, 140(6): 2928-2931, 1999, (IDS) thereafter referred as Upton 1999] in view of Nagano et al [JBC, 267(34): 24863-24870, 1992) (IDS)]; Nakao et al (US 5,360,789; date issued; May 20, 1993); Schvartz et al (The International Journal of Biochemistry & Cell Biology

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31: 539-544, 1999); of Klemke et al, (The Journal of Cell Biology, 127: 859-866, 1994 (IDS)) is withdrawn in view of the amendment to the claims dated 06/07/2011.

Applicant's arguments are convincing in view of the amendment.

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Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner

should be directed to MAGDALENE K. SGAGIAS whose telephone number is (571)272-3305.

The examiner can normally be reached on 8.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Paras Peter can be reached on 571-272-4517. The fax phone number for the

organization where this application or proceeding is assigned is 571-273-8300. Information

regarding the status of an application may be obtained from the Patent Application Information

Retrieval (PAIR) system. Status information for published applications may be obtained from

either Private PAIR or Public PAIR. Status information for unpublished applications is available

through Private PAIR only. For more information about the PAIR system, see http://pair-

direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the

Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from

a USPTO Customer Service Representative or access to the automated information system,

call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Magdalene K. Sgagias,

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/Thaian N Ton/

Primary Examiner, Art Unit 1632